

Application No. 10/532,033
AMENDMENT dated April 6, 2010
Response to the Office Action of January 13, 2010

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Canceled)

2. (Previously Presented) The method of claim 16 wherein:

R¹ is selected from the group consisting of hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, and substituted or unsubstituted alkynyl, wherein when R¹ is substituted alkyl, substituted alkenyl, or substituted alkynyl, the substituent(s) thereof is (are) selected from the group consisting of alkoxy, haloalkoxy, alkylthiol, halogen, unsubstituted phenyl, and phenyl substituted with a moiety selected from the group consisting of alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthiol, and halogen;

R² and R³ are independently selected from the group consisting of R¹, alkoxy, alkoxyalkyl, benzyloxy, cyano, and alkylcarbonyl;

R⁴ is selected from the group consisting of:

(a) substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, and substituted or unsubstituted alkynyl, wherein when R⁴ is substituted alkyl, substituted alkenyl, or substituted alkynyl, the substituent(s) thereof is (are) selected from the group consisting of an alkoxy, haloalkoxy, alkylthiol, a halogen, unsubstituted phenyl, and phenyl substituted with a

Application No. 10/532,033
AMENDMENT dated April 6, 2010
Response to the Office Action of January 13, 2010

moiety selected from the group consisting of alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthiol, and halogen;

(b) hydroxyl;

(c) halogen;

(d) cyano;

(e) acyl, amine, monoalkylamine, dialkylamine, unsubstituted phenyl, and phenyl substituted with a moiety selected from the group consisting of alkyl, haloalkyl, alkoxy, haloalkoxy, and alkylthiol;

$m = 0$ or 1 ;

when it is present, R^5 is a group having the same definition as that given above for R^4 ,

A is a direct bond, -O-, -S-, -NR⁹-, -CHR⁷- or -O-CHR⁷-,

each R⁹, when any are present, is selected from the group consisting of hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, and substituted or unsubstituted alkynyl, wherein when an R⁹ is a substituted alkyl, a substituted alkenyl, or a substituted alkynyl, the substituent(s) thereof is (are) selected from the group consisting of alkoxy, haloalkoxy, alkylthiol, halogen, unsubstituted phenyl, and phenyl substituted with a moiety selected from the group consisting of alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthiol, and halogen;

R⁷ is selected from the group consisting of R⁹; hydroxyl; halogen; cyano; acyl; alkoxy; haloalkoxy; and alkylthiol;

Application No. 10/532,033
AMENDMENT dated April 6, 2010
Response to the Office Action of January 13, 2010

A is linked to the 4-position of the benzene ring M; and

R⁶ is a substituted or unsubstituted phenyl or an aromatic heterocycle which when R⁶ is a substituted phenyl or substituted aromatic heterocycle, the substituent(s) thereof is (are) selected from the group consisting of

- (a) hydroxyl;
- (b) halogen;
- (c) cyano;
- (d) acyl;
- (e) amine;
- (f) alkylamine;
- (g) dialkylamine;
- (h) alkyl;
- (i) haloalkyl;
- (j) R^aO-alkyl;
- (k) acyloxyalkyl;
- (l) cyanooxyalkyl;
- (m) alkoxy;
- (n) haloalkoxy;
- (o) alkylthiol;

Application No. 10/532,033
AMENDMENT dated April 6, 2010
Response to the Office Action of January 13, 2010

(p) cycloalkyl unsubstituted or substituted with a moiety selected from the group consisting of alkyl, haloalkyl, alkoxy, haloalkoxy, and alkylthiol; and

(q) benzyl unsubstituted or substituted with a moiety selected from the group consisting of alkyl, haloalkyl, alkoxy, haloalkoxy, and alkylthiol.

3. (Previously Presented) The method of claim 16 wherein:

$R^1 = H$

R^2 , R^3 , R^4 , and R^5 are independently selected from the group consisting of C_1 - C_6 alkyl and R^5 is linked to the carbon at C_5 of the benzyl ring M, with $m=1$;

A is linked to the carbon at C_4 of the benzyl ring M and represents -O-; and

R^6 is unsubstituted aryl or aryl substituted with at least one moiety selected from the group consisting of alkyl and halogen.

4. (Previously Presented) The method of claim 3 wherein compound (I) is selected from the group consisting of

N-ethyl-N-methyl-N'-[4-(4-

chloro-3-trifluoromethylphenoxy)-2,5-dimethylphenyl]imidoformamide,

N-ethyl-N-methyl-N'-[4-(4-

fluoro-3-trifluoromethylphenoxy)-2,5-dimethylphenyl]imidoformamide,

Application No. 10/532,033
AMENDMENT dated April 6, 2010
Response to the Office Action of January 13, 2010

N-ethyl-N-methyl-N'-[4-(4-cyano-3-trifluoromethylphenoxy)-2,5-dimethylphenyl]imidoformamide,
and the possible tautomers and salts that are pharmaceutically acceptable of these compounds (I).

5. (Previously Presented) The method of claim 16 wherein the medicament further comprises at least one other antifungal compound (II) selected from the group consisting of azoles; polyenes; allylamines and benzylamines; thiocarbamates; candins; nucleoside analogues; sordarins; polyoxines and nikkomycins; pradimicins; benanomycins; aureobasidins; UK-2A or UK-3A; and cationic peptides; taken alone or as a mixture, and their possible tautomers and salts and their lipid or liposomal formulations that are pharmaceutically acceptable.

6. (Canceled)

7. (Previously Presented) The method of claim 17 wherein the mass ratio (I/II) is $0.02 \leq I/II \leq 50$.

8. (Previously Presented) The method of claim 17 wherein the compound (I)/compound (II) ratio is chosen so as to produce a synergistic effect.

Application No. 10/532,033
AMENDMENT dated April 6, 2010
Response to the Office Action of January 13, 2010

9. (Previously Presented) The method of claim 8 wherein the compound (I)/compound (II) ratio is between 0.5 and 10.

10. (Previously Presented) The method of claim 16 wherein the medicament further comprises at least one pharmaceutically acceptable excipient.

11. (Previously Presented) The method of claim 9 wherein the medicament comprises from 0.5 to 99% of the combination of compound (I) and compound (II).

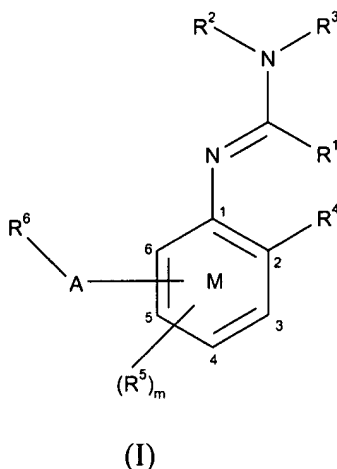
12-13. (Canceled)

14. (Previously Presented) The method of claim 16 wherein the infection is an *Candida albicans* infection.

15. (Previously Presented) The method of claim 16 wherein the infection is an *Aspergillus fumigatus* infection.

16. (Previously Presented) A method for treating *Candida albicans* or *Aspergillus fumigatus* infections in humans comprising administering to a human patient in need of such treatment a

pharmaceutically effective dose of an antifungal medicament comprising at least one compound of formula (I):



wherein:

R¹ is selected from the group consisting of hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and a substituted or unsubstituted carbocyclic or heterocyclic monovalent group;

R² and R³ are independently selected from the group consisting of R¹; a cyano; an acyl; -OR^a or -SR^a, wherein R^a is selected from the group consisting of a substituted or unsubstituted alkyl, a substituted or unsubstituted alkenyl, a substituted or unsubstituted alkynyl, and a substituted or unsubstituted carbocyclic or heterocyclic monovalent group, or R² and R³, or R² and R¹ may form together and with the atoms linking them, a substituted or unsubstituted ring;

R⁴ is selected from the group consisting of a substituted or unsubstituted alkyl, a substituted or unsubstituted alkenyl, a substituted or unsubstituted alkynyl, a substituted or

Application No. 10/532,033
AMENDMENT dated April 6, 2010
Response to the Office Action of January 13, 2010

unsubstituted carbocyclic or heterocyclic monovalent group, hydroxyl, mercapto, azido, nitro, halo, cyano, unsubstituted or substituted acyl, amino, cyanato, thiocyanato, $-\text{SF}_5$, $-\text{OR}^a$, $-\text{SR}^a$, and $-\text{Si}(\text{R}^a)_3$;

$m = 0, 1, 2$ or 3 ;

the optional R^5 group or the optional R^5 groups, which may be mutually identical or different, have the same definition as that given above for R^4 ;

R^6 is an unsubstituted or substituted carbocyclic or heterocyclic group; and

A is selected from the group consisting of a direct bond, $-\text{O}-$, $-\text{S}(\text{O})_n-$, $-\text{NR}^9-$, $-\text{CR}^7=\text{CR}^7-$, $-\text{C}\equiv\text{C}-$, $-\text{A}^1-$, $-\text{A}^1-\text{A}^1$, $-\text{O}-(\text{A}^1)_k-\text{O}-$, $-\text{O}-(\text{A}^1)_k-$, $-\text{A}^3-$, $-\text{A}^4-$, $-\text{A}^1\text{O}-$, $-\text{A}^1\text{S}(\text{O})_n-$, $-\text{A}^2-$, OA^2- , $-\text{NR}^9\text{A}^2-$, $-\text{OA}^2-\text{A}^1-$, $-\text{OA}^2-\text{C}(\text{R}^7)=\text{C}(\text{R}^8)-$, $-\text{S}(\text{O})_n\text{A}^1-$, $-\text{A}^1-\text{A}^4-$, $-\text{A}^1-\text{A}^4-\text{C}(\text{R}^8)=\text{N}-\text{N}=\text{CR}^8-$, $-\text{A}^1-\text{A}^4-\text{C}(\text{R}^8)=\text{N}-\text{X}^2-\text{X}^3-$, $-\text{A}^1-\text{A}^4-\text{A}^3-$, $-\text{A}^1-\text{A}^4-\text{N}(\text{R}^9)-$, $-\text{A}^1-\text{A}^4-\text{X}-\text{CH}_2-$, $-\text{A}^1-\text{A}^4-\text{A}^1-$, $-\text{A}^1-\text{A}^4-\text{CH}_2\text{X}-$, $-\text{A}^1-\text{A}^4-\text{C}(\text{R}^8)=\text{N}-\text{X}^2-\text{X}^3-\text{X}^1-$, $-\text{A}^1-\text{X}-\text{C}(\text{R}^8)=\text{N}-$, $-\text{A}^1-\text{X}-\text{C}(\text{R}^8)=\text{N}-\text{N}=\text{CR}^8-$, $-\text{A}^1-\text{X}-\text{C}(\text{R}^8)=\text{N}-\text{N}(\text{R}^9)-$, $-\text{A}^1-\text{X}-\text{A}-\text{X}^1-$, $-\text{A}^1-\text{O}-\text{A}^3-$, $-\text{A}^1-\text{O}-\text{C}(\text{R}^7)=\text{C}(\text{R}^8)-$, $-\text{A}^1-\text{O}-\text{N}(\text{R}^9)-\text{A}^2-\text{N}-$ (R^9)-, $-\text{A}^1-\text{O}-\text{N}(\text{R}^9)-\text{A}^2-$, $-\text{A}^1-\text{N}(\text{R}^9)-\text{A}^2-\text{N}(\text{R}^9)-$, $-\text{A}^1-\text{N}(\text{R}^9)-\text{A}^2-$, $-\text{A}^1-\text{N}(\text{R}^9)-\text{N}=\text{C}(\text{R}^8)-$, $-\text{A}^3-\text{A}^1-$, $-\text{A}^4-\text{A}^3-$, $-\text{A}^2-\text{NR}^9-$, $-\text{A}^1-\text{A}^2-\text{X}^1-$, $-\text{A}^1-\text{A}^1-\text{A}^2-\text{X}^1-$, $-\text{O}-\text{A}^2-\text{N}(\text{R}^9)-\text{A}^2-$, $-\text{CR}^7=\text{CR}^7-\text{A}^2-\text{X}^1-$, $-\text{C}\equiv\text{C}-\text{A}^2-\text{X}^1-$, $-\text{N}=\text{C}(\text{R}^8)-\text{A}^2-\text{X}^1-$, $-\text{C}(\text{R}^8)=\text{N}-\text{N}=\text{C}(\text{R}^8)-$, $-\text{C}(\text{R}^8)=\text{N}-\text{N}(\text{R}^9)-$, $-(\text{CH}_2)_2-\text{O}-\text{N}=\text{C}(\text{R}^8)-$ and $-\text{X}-\text{A}^2-\text{N}(\text{R}^9)-$

wherein

$n = 0, 1$ or 2 ,

Application No. 10/532,033
AMENDMENT dated April 6, 2010
Response to the Office Action of January 13, 2010

$k = 1$ to 9 ,

$A^1 = -CHR^7-$,

$A^2 = -C(=X)-$,

$A^3 = -C(R^8)=N-O-$,

$A^4 = -O-N=C(R^8)-$,

$X = O$ or S ,

$X^1 = O$, S , NR^9 or a direct bond,

$X^2 = O$, NR^9 or a direct bond,

$X^3 = \text{hydrogen}$, $-C(=O)-$, $-SO_2-$ or a direct bond,

each R^7 is independently selected from the group consisting of unsubstituted or substituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted phenyl, hydrogen, halogen, cyano, and acyl;

each R^8 is independently selected from the group consisting of alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkylthio, a substituted or unsubstituted carbocyclic or heterocyclic monovalent group, and hydrogen;

each R^9 is independently selected from the group consisting of unsubstituted or substituted alkyl, a substituted or unsubstituted monovalent carbocyclic or heterocyclic group, and acyl; or two R^9 groups may form together, and with the atoms linking them, a 5-7-membered ring;

Application No. 10/532,033
AMENDMENT dated April 6, 2010
Response to the Office Action of January 13, 2010

the group represented on the right side of the bond A is linked to R⁶;

or -A-R⁶ and R⁵ form together with the benzene ring M, a system of unsubstituted or substituted condensed rings;

and optical and/or geometric isomers, tautomers and salts of (I) with an acid or a base that are pharmaceutically acceptable;

and mixtures thereof.

17. (Previously Presented) The method of claim 5 wherein compound (I) is selected from the group consisting of N-ethyl-N-methyl-N'-[4-(4-chloro-3-trifluoromethylphenoxy)-2,5-dimethylphenyl]imidoformamide and N-ethyl-N-methyl-N'-[4-(4-cyano-3-trifluoromethylphenoxy)-2,5-dimethylphenyl]imidoformamide and compound (II) is selected from the group consisting of fluconazole and itraconazole.

18-19. (Canceled)

20. (Previously Presented) The method of claim 11 wherein the infection is an *Candida albicans* infection.

21. (Previously Presented) The method of claim 11 wherein the infection is an *Aspergillus fumigatus* infection.

Application No. 10/532,033

AMENDMENT dated April 6, 2010

Response to the Office Action of January 13, 2010

22. (New) The method of claim 20 wherein compound (I) is N-ethyl-N-methyl-N'-[4-(4-chloro-3-trifluoromethylphenoxy)-2,5-dimethylphenyl]imidoformamide and compound (II) is fluconazole.

23. (New) The method of claim 21 wherein compound (I) is N-ethyl-N-methyl-N'-[4-(4-chloro-3-trifluoromethylphenoxy)-2,5-dimethylphenyl]imidoformamide and compound (II) is itraconazole.